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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,014	REMACLE ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *March 24, 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,9,10,12-23,38,40 and 42-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,9,10,12-23,38,40 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants response, filed on March 24, 2004. Currently, claims 1-2, 4, 9-10, 12-23, 38, 40, and 42-45 are pending. This action contains new rejections necessitated by Applicants' amendments, and is made FINAL. For example, Applicants' amended Claim 1 to recite, "detecting a nucleotide sequence *specific* of said organism," "capture nucleotide sequences being *covalently* bound in an array," and "capture nucleotide sequences comprise a nucleotide sequence of about *15* to about *40* bases." (emphasis added to show amendments) Any objections and rejections not reiterated below are hereby withdrawn. Specifically, the 103 and 112, 2nd paragraph rejections have been withdrawn in view of Applicants' amendments. Furthermore, all of Applicants arguments are directed to rejections no longer maintained, and accordingly, are not persuasive in view of the new rejections below.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-2, 4, 9-10, 12-23, 38, 40, and 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-2, 4, 9-10, 12-23, 38, 40, and 42-45 are indefinite over "a nucleotide sequence specific of said organism" because it is not clear as to what constitutes "a nucleotide sequence specific of an organism." For example, it is not clear as to whether the nucleotide sequence is only found in the particular organism and no other organism or it shared by a specific group of organisms, etc. The specification does not define or teach what is encompassed by a "a nucleotide sequence specific of an organism."

B) Claims 1-2, 4, 9-10, 12-23, 38, 40, and 42-45 are indefinite over "presents a homology higher than 60%" because it is not clear as to what "homology" refers to in this context (e.g., sequence identity, whether the sequences are from the same genus, etc.). Furthermore, it is not clear as to what is meant by "presents" a homology.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161).

Regarding Claims 1, 10, 38, 42 and 45, Anthony teaches a for identifying and/or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence specific of said organism, wherein said specific nucleotide sequence presents a homology higher than 60% with at least 4 other homologous nucleotide sequences from other organisms comprising:

amplifying or copying said specific nucleotide sequence into target nucleotide sequence using primer pairs which are capable of amplifying at least two of said homologous nucleotide sequences from other organisms (e.g., primers capable of amplifying 23S rDNA from bacterial samples) (page 782); contacting said target nucleotide sequence with single-stranded capture nucleotide sequences (Table 2, page 783), said single-stranded capture nucleotide sequences being covalently bound in an array to an insoluble solid support (page 783, 2nd column) (teaching the probes were cross-linked to the membrane), wherein said array comprises

at least 4 different bound single-stranded capture nucleotide sequences/cm^2 of solid support surface (page 783 and 785) and wherein said stranded capture nucleotide sequences comprise a nucleotide sequence of about 15 to about 40 bases which is able to specifically bind to said target nucleotide sequence without binding to said at least 4 homologous nucleotide sequences (Table 2 and pages 786-787); and

detecting specific hybridization of said target nucleotide sequence to said capture nucleotide sequences (pages 784-787).

Specifically, Anthony teaches using a universal primer pair to amplify sequences from bacteria present, and then hybridizing the amplification products to specific capture probes on an oligonucleotide array (see pages 781-783). Anthony teaches this method is useful in discriminating various bacterial species and groups (see, for example, page 784, 2nd column). Anthony also teaches this method can be used in a wide variety of discrimination assays, the method can be automated, and can be further improved by using larger arrays.

Anthony does not teach the use of a spacer that is at least 6.8 nm in length.

However, Shchepinov et al. teaches the advantages of covalently binding capture probes to an insoluble support via a spacer (see abstract and pages 1155, 1160 and 1161). Specifically, Shchepinov teaches the use of spacers helps increase hybridization yields, enabling a more effective and efficient hybridization assay (see abstract and pages 1155, 1160 and 1161). Shchepinov teaches the use of various sized spacers, including those of at least 6.8 nm in length (see pages 1156-1161).

In view of the teachings of Shchepinov, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and

so as to have used a spacer of at least 6.8 nm in length. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony in order to have achieved the benefits stated by Shchepinov of increasing the kinetics of hybridization, thus providing a more effective and efficient means of hybridization/detection.

Regarding Claim 2, Anthony teaches the amplified nucleotide sequence is DNA (page 782).

Regarding Claims 9 and 40, Anthony teaches the density of the capture nucleotide sequence bound to the surface at a specific location is more than about 10-100 fmoles per cm^2 of solid support surface (pages 782-785).

Regarding Claims 12 and 44, Anthony teaches other primers can be used (pages 782-783).

Regarding Claim 13, Shchepinov teaches the insoluble solid support is a plastic (page 1156).

Regarding Claims 16 and 17, Anthony teaches the solid support also bears capture nucleotide sequences specific of the homologous sequences specific for the binding with the homologous target nucleotide sequence together with a consensus sequence able to bind to said target nucleotide sequence and to said at least 4 homologous nucleotide sequences, as well as, Staphylococcus genus identification using a specific capture sequence with a consensus sequence, and that the homologous sequences differ (see Table 2 and pages 782-784).

Regarding Claim 43, Shchepinov teaches that non-specific spacers of at least 20 nucleotides can be used (pages 1160-1161).

8. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Vannuffel et al. (WO 99/16780, cited in the IDS).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the *FemA* gene of Staphylococci species.

However, Vannuffel teaches the detection of the *FemA* gene of *Staphylococci* species is advantageous in detecting and diagnosing staphylococcal infections and for determining drug resistance (see abstract, and pages 1-5, 8-13 and Examples 1-7). Vannuffell teaches the detection of several *Staphyloccal* species, such as *S. hominis, S. saprophyticus, S. epidermidis* and *S. haemolyticus* (pg. 4), and other gram-positive bacteria (pgs. 5 and 10).

Accordingly, in view of the teachings of Vannuffel, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to have identified and/or quantified the *FemA* sequence of *Staphylococcal* species. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of providing an effective means of detecting specific species of the *Staphylococci* genus for use in diagnosing staphylococcal infections or for determining drug resistance.

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Boon et al. (USPN 6,488,932).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the MAGE family.

However, Boon teaches that is advantageous to detect individual sequences that belong to the MAGE family (which are closely related) for the diagnosis of tumors, (See Fig. 4 and cols. 3-8, for example).

Accordingly, in view of the teachings of Boon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to detect a sequence belonging to the MAGE family. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of providing an effective means of diagnosing a tumor.

10. Claims 4, 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Apple et al. (USPN 5,451,512).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the HLA-A family.

However, Apple teaches that is advantageous to detect individual sequences that belong to the HLA-A family (which are closely related) to help determine potential transplantation donors, thus aiding in minimizing the risk of transplantation rejection. (See cols. 1-8, for

example). Regarding Claims 4 and 14, Apple teaches the amplified nucleotide sequences can be mRNA first reverse transcribed into cDNA (see cols. 4-7, for example).

Accordingly, in view of the teachings of Apple, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to detect a sequence belonging to the HLA-A family. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of minimizing the risk of transplantation rejection.

11. Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Klein et al. (USPN 6,255,059).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the dopamine or histamine receptors coupled to the G genes family.

However, Klein teaches that is advantageous to detect sequences that belong to the dopamine or histamine receptors coupled to the G genes family (which are closely related) to mediate transmembrane signaling by external stimuli, endocrine function, carbohydrate metabolism, etc. (see cols. 1-4, for example)

Accordingly, in view of the teachings of Klein, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to detect a sequence belonging to the dopamine or histamine

receptors coupled to the G genes family. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of mediating transmembrane signaling for many vital biological processes, such as carbohydrate metabolism.

12. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc. Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Murphy et al. (WO/9405695).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the choline receptors coupled to the G genes family.

However, Murphy teaches that is advantageous to detect sequences that belong to the choline receptors coupled to the G genes family (which are closely related) for use in diagnosis of neurological, viral or endocrine pathologies. (See pgs. 12-16 and 26-34, for example).

Accordingly, in view of the teachings of Murphy, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to detect a sequence belonging to the choline receptors coupled to the G genes family. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of diagnosing neurological, viral or endocrine pathologies.

13. Claims 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anthony et al. (J of Clin. Microbio. (2000) 38(2): 781-788, cited in the IDS), in view of Shchepinov et al. (Nuc.

Acid Res. (1997) 25(6): 1155-1161), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Waxman et al. (USPN 6,207,648).

The teachings of Anthony and Shchepinov are presented above. The references do not teach the sequence to be identified belongs to the cytochrome P450 isoforms family.

However, Waxman teaches that is advantageous to detect sequences that belong to the cytochrome P450 isoforms family (e.g., 2D6 and 2C19, which are closely related) for use in treatment of cancer (see cols. 3-8, 15-25 and Examples).

Accordingly, in view of the teachings of Waxman, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Shchepinov so as to detect a sequence belonging to the cytochrome P450 isoforms family. One of ordinary skill in the art would have been motivated to modify the teachings of Anthony and Shchepinov in order to have achieved the benefit of identifying cytochrome P450 isoforms, which can be used in developing and providing anti-cancer drugs for use in treating cancer.

Conclusion

14. No claims are allowable.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler
July 26, 2004

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